# PATENT COOPERATION TREATY



From the INTERNATIONAL SEARCHING AUTHORITY

| To: WOLF, GREENFIELD & SACKS, P.C. Attn. Plumer, Elizabeth R. 600 Atlantic Avenue Federal Reserve Plaza Boston, Massachusetts 02210 UNITED STATES OF AMERICA |
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| o: WOLF, GREENFIELD & SACKS, P.C. Attn. Plumer, Elizabeth R. 600 Atlantic Avenue Federal Reserve Plaza Boston, Massachusetts 02210 UNITED STATES OF AMERICA  | ГОИ<br>І ЭНТ   | TIFICATION OF T<br>NTERNATIONAL<br>OR THE DE   | SEARCH REPORT<br>CLARATION                 |
|--|--|--|--|
|  | Date of mailing (day/month/year)   | 21/01/199  | 8  |
| Applicant's or agent's file reference<br>IO254/7007WO  | FOR FURTHER  | ACTION Se  | e paragraphs 1 and 4 below                 |
| International application No. PCT/US 97/11279  | International filing<br>(day/month/year)   | date<br>27/06/199  | 7  |
| Applicant _  |  |  | DOCKETED                                   |
| TRUSTEES OF TUFTS COLLEGE et al.   |  |  | JAN 2 9 1998                               |
| Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the clair  When? The time limit for filing such amendments is norm International Search Report; however, for more of  Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.3  For more detailed instructions, see the notes on the acc  2. The applicant is hereby notified that no International Sear Article 17(2)(a) to that effect is transmitted herewith.  | ally 2 months from the letails, see the notes  5  ompanying sheet.   | on the accompanying file Folder (2) Electronic Code Docket Entry 3 Docket Cross O Order Copies Annuities Other | ng sheet. INITIAL Book D                   |
| 3. With regard to the protest against payment of (an) additional the protest together with the decision thereon has be applicants's request to forward the texts of both the protest; the a  | en transmitted to the<br>protest and the decis   | International Burea<br>ion thereon to the de   | uu together with the<br>esignaled Offices. |
| 4. Further action(s): The applicant is reminded of the following Shortly after 18 months from the priority date, the international If the applicant wishes to avoid or postpone publication, a not priority claim, must reach the International Bureau as provide completion of the technical preparations for international publication 19 months from the priority date, a demand for international wishes to postpone the entry into the national phase until 30 within 20 months from the priority date, the applicant must permit the priority date. | application will be poice of withdrawal of the distribution of the distribution on all preliminary examenths from the prior of the prio | mination must be file<br>rity date (in some Of   | ed if the applicant fices even later).     |
| Within 20 months from the priority date, the applicant must per before all designated Offices which have not been elected in priority date or could not be elected because they are not both   | and by Chapter II.   |  |  |

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, \_ Fax: (+31-70) 340-3016

A. Overbeeke

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PCT/US 97/11279

A CLASSIFICATION OF SUBJECT MATTER 1PC 6 CO7K14/47 CO7K14/435 C07K14/535 \_\_C07F5/02 C07K14/16 A61K31/69 A61K38/16

According to International Patent Classification (IPC) or to both national classification and IPC

### B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 6 C07K C07F A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| X          | WO 95 15309 A (FERRING BV ; JENKINS PAUL D (GB); JONES D MICHAEL (GB); SZELKE MICH) 8 June 1995 see page 1, paragraph 4 - page 3, paragraph 10 see page 4, paragraph 4; claims; examples; table 7 | 1-16,<br>35-59        |
| Å          | WO 95 29190 A (PASTEUR INSTITUT) 2 November 1995 see page 26, paragraph 4 - page 27, paragraph 1; claims; examples  | 1-16,<br>35-59        |
| A          | US 5 329 028 A (ASHKENAZI AVI J ET AL) 12 July 1994 see column 2, line 63 - column 3, line 23; claims; examples   | 1,39-41               |

| *Special categories of cited documents:  *A* document defining the general state of the art which is not considered to be of particular relevance  *E* earlier document but published on or after the international filling date  *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  *O* document referring to an oral disclosure, use, exhibition or other means  *P* document published prior to the international filling date but | To later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "&" document member of the same patent family |  |  |  |  |
|---|--|--|--|--|--|
| later than the priority date claimed  Date of the actual completion of the international search   | Date of mailing of the international search report   |  |  |  |  |
| 7 January 1998  | 2 1. 01. 98  |  |  |  |  |
| Name and mailing address of the ISA   | Authorized officer   |  |  |  |  |
| European Patent Office, P.B. 5818 Patentiaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016   | Fuhr, C  |  |  |  |  |

Form PCT/ISA/210 (second sheet) (July 1992)

Y Further documents are listed in the continuation of box C.

X Patent family members are listed in annex.

# INT NA NAL SEARCH REPORT

ernational cation No
PCT/US 97/11279

|            |   | PCT/US 97 | 711275                | $\dashv$ |
|------------|---|-----------|-----------------------|----------|
|            | otion) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages  | 77,       | Relevant to claim No. | $\dashv$ |
| Category * | Citation of document, with indication, where appropriate, or side to the angle of the comment.  |           |                       | $\dashv$ |
| A          | J. Wijdenes et al. 'Monoclonal Antibodies (mAb) against GP130 imitating Cytokines which use the gp130 for Signal Transduction' in: The 9th International Congress of Immunology, Abstract Book, 23-29 July, 1995, San Francisco, CA, USA XP002051385 abstract no. 1794 on page 303 see abstract |           | 1                     |          |
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# INT' NAT AL SEARCH REPORT

Information on patent family members

mational ation No PCT/US 97/11279

| Patent document<br>cited in search report | Publication date | Patent family<br>member(s)  | Publication<br>date  |
|---|------------------|---|--|
| WO 9515309 A                              | 08-06-95         | AU 1113395 A CA 2178066 A CN 1141033 A CZ 9601595 A EP 0731789 A FI 962315 A HU 76274 A JP 9509921 T NO 962269 A PL 314838 A ZA 9409525 A | 19-06-95<br>08-06-95<br>22-01-97<br>15-01-97<br>18-09-96<br>05-08-96<br>28-07-97<br>07-10-97<br>30-07-96<br>30-09-96<br>02-08-95 |
| WO 9529190 A                              | 02-11-95         | FR 2719049 A<br>AU 2412595 A<br>CA 2188470 A<br>EP 0756603 A  | 27-10-95<br>16-11-95<br>02-11-95<br>05-02-97   |
| US 5329028 A                              | 12-07-94         | US 5605791 A  | 25-02-97   |

## PATENT COOPERATION TREATY

# **PCT**

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference  | (Form PCT/ISA/22  | Transmittal of International Search Report<br>20) as well as, where applicable, item 5 below. |
|--|---|---|
| I0254/7007W0   | ACTION  | (Earliest) Priority Date (day/month/year)   |
| International application No.  | International filing date (day/month/year)  | '   |
| PCT/US 97/11279  | 27/06/1997  | 11/04/1997  |
| Applicant  |   |   |
| TRUSTEES OF TUFTS COLLEGE  | et al.  |   |
| This International Search Report has bee according to Article 18. A copy is being tr | en prepared by this International Searching Auth<br>ansmitted to the International Bureau.  | nority and is transmitted to the applicant  |
| This International Search Report consists  X It is also accompanied by a cop         | s of a total of sheets.  by of each prior art document cited in this report.  |   |
| 1. X Certain claims were found un  | searchable (see Box I).   |   |
| 2. Unity of Invention is lacking (   | see Box II).  |   |
| 3. X The international application co  | ontains disclosure of a nucleotide and/or amin  | o acid sequence listing and the   |
| international search was carried   | d out on the basis of the sequence listing ed with the international application.   |   |
|  | nished by the applicant separately from the inte  | mational application,   |
|  | but not accompanied by a statement to the matter going beyond the disclosure in the   | ne effect that it did not include   |
| Tra  | anscribed by this Authority   | ·   |
| 4. With regard to the title, X the   | e text is approved as submitted by the applicant  |   |
| 1  | e text has been established by this Authority to r  |   |
|  |   |   |
|  |   |   |
| 5. With regard to the abstract,  |   |   |
| X the  | e text is approved as submitted by the applicant  | <b>.</b>  |
| th B   | e text has been established, according to Rule 3<br>ox III. The applicant may, within one month from<br>earch Report, submit comments to this Authority | 38.2(b), by this Authority as it appears in<br>I the date of mailing of this International    |
| 6 The faces 400  | Wichard with the chatrest in  |   |
| 6. The figure of the drawings to be pu   | blished with the abstract is:<br>s suggested by the applicant.  | X None of the figures.  |
|  | s suggested by the applicant.  ecause the applicant failed to suggest a figure.   |   |
| _  | ecause this figure better characterizes the inven   | ition.  |
|  | •   |   |

# International application No. PCT/US 97/11279

### INTERNATIONAL SEARCH REPORT

Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) Box I This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: see FURTHER INFORMATION sheet PCT/ISA/210 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: Claims Nos.: see FURTHER INFORMATION sheet PCT/ISA/210 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). Claims Nos.: Box II Observations where unity of Invention is lacking (Continuation of item 2 of first sheet) This International Searching Authority found multiple inventions in this international application, as follows: As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: The additional search fees were accompanied by the applicant's protest. Remark on Protest No protest accompanied the payment of additional search fees.

#### NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

## INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international polication. Furthermore, it should be emphasized that provisional protection is available in some States only.

### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

#### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; If the language of the international application is French, the letter must be in French.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

Claims Nos.: 1-7, 9-10, 16-23, 25-26, 29-31, 35-59

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

In view of the extremely large number of compounds falling under claims 1-7, 9-10, 16-23, 25-26, 29-31, 35-38, 49-51, 58-59 and claims 39-48, 52-57 referring to them and of the absence of any technical support for these compounds in the description, the ISA considers that it is not economically reasonable to draw a search report covering the entire subject matter characterized above.

The search has therefore been

limited to the real examples given in the description and closely related ones and includes compounds having the alleged activities.

Remark: As far as claims 39-43, 45-48 and 55-57 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.

#### NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
   \*Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
   claims 30, 33 and 36 unchanged; new claims 49 to 51 added.
- [Where originally there were 15 claims and after amendment of all claims there are 11]: \*Claims 1 to 15 replaced by amended claims 1 to 11.\*
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
   "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
   "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

#### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Adide 19(1))

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# FATENT COOPERATION TREA



| From the INTERNATIONAL SEARCHING AUTHORITY   | ** PCT   |
|--|--|
| 600 Atlantic Avenue Electronic Code Book   | NOTIFICATION OF TRANSMITTAL OF INITIAL THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION  (PCT Rule 44.1)   |
|  | (day/month/year) 13/08/1998  |
| Applicant's or agent's file reference  I 0254/7005W0  International application No.  | FOR FURTHER ACTION See paragraphs 1 and 4 below  International filing date (day/month/year) 30/04/1998   |
| PCT/US 98/08838 Applicant  | 30/04/1990   |
| TRUSTEES OF TUFTS COLLEGE  |  |
| 1. X  The applicant is hereby notified that the International Search Filling of amendments and statement under Article 19 The applicant is entitled, if he so wishes, to amend the claim When? The time limit for filing such amendments is norma International Search Report; however, for more de Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.35  For more detailed instructions, see the notes on the account of the applicant is hereby notified that no International Search Article 17(2)(a) to that effect is transmitted herewith.  | is of the International Application (see Rule 46):  Illy 2 months from the date of transmittal of the stails, see the notes on the accompanying sheet.   |
| 3. With regard to the protest against payment of (an) addition the protest together with the decision thereon has bee applicants's request to forward the texts of both the protest together.  | onal fee(s) under Rule 40.2, the applicant is notified that:<br>in transmitted to the International Bureau together with the<br>otest and the decision thereon to the designated Offices.  |
| no decision has been made yet on the protest; the app  | plicant will be notified as soon as a decision is made.  |
| 4. Further action(s): The applicant is reminded of the following:  Shortly after 18 months from the priority date, the international a If the applicant wishes to avoid or postpone publication, a notice priority claim, must reach the International Bureau as provided completion of the technical preparations for international public.  Within 19 months from the priority date, a demand for internation wishes to postpone the entry into the national phase until 30 mm.  Within 20 months from the priority date, the applicant must perform all designated Offices which have not been elected in the priority date or could not be elected because they are not bound. | in Rules 90 bis.1 and 90 bis.3, respectively, before the ation.  In all preliminary examination must be filed if the applicant onths from the priority date (in some Offices even later).  Form the prescribed acts for entry into the national phase the demand or in a later election within 19 months from the d by Chapter II. |
| Name and mailing address of the International Searching Authority  European Patent Office, P.B. 5818 Patentiaan 2  NL-2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  Fax: (+31-70) 340-3016   | Authorized officer Mike Iverstam   |

# PATENT COOPERATION TRE /

# PCT

# INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference 10254/7005W0                                   | FOR FURTHER see Notification o (Form PCT/ISA/2  | f Transmittal of International Search Report<br>20) as well as, where applicable, item 5 below. |
|--|---|---|
| International application No.  | International filing date (day/month/year)  | (Earliest) Priority Date (day/month/year)   |
| PCT/US 98/08838  | 30/04/1998  | 07/05/1997  |
| Applicant  |   |   |
| TRUSTEES OF TUFTS COLLEGE  |   |   |
| This International Search Report has bee according to Article 18. A copy is being to | on prepared by this International Searching Authors ansmitted to the International Bureau.  | nority and is transmitted to the applicant  |
| This International Search Report consists  It is also accompanied by a cop           | s of a total of <u>4</u> sheets.<br>by of each priorant document cited in this report   | -   |
| 1. X Certain claims were found ur  | nsearchable(see Box I).   |   |
| 2. Unity of invention is lacking(  | see Box II).  |   |
| 3. The international application of  | ontains disclosure of a nucleotide and/or amin<br>d out on the basis of the sequence listing  | o acid sequence listing and the   |
| •  | d with the international application.   |   |
|  | nished by the applicant separately from the inte  | rnational application,  |
|  | but not accompanied by a statement to the matter going beyond the disclosure in the   | he effect that it did not include<br>e international application as filed.                      |
| Tr.  | anscribed by this Authority   |   |
|  | e text is approved as submitted by the applican   |   |
|  | e text has been established by this Authority to  |   |
| POTENTIATION OF THE CYTOPLASMIC DIPEPTION  | IMMUNE RESPONSE THROUGH DELI<br>ASE   | VERY OF COMPOUNDS BINDING A   |
|  |   |   |
| 5. With regard to the abstract,  | the applicant   | It  |
|  | e text is approved as submitted by the applican<br>e text has been established, according to Rule<br>ox III. The applicant may, within one month from | 38.2(b), by this Authority as it appears in   |
| Se   | earch Report, submit comments to this Authorit  | y. `  |
| 6. The figure of the drawings to be pu   | blished with the abstract is:   | [ ] N   |
| Figure No as   | s suggested by the applicant.   | X None of the figures.  |
|  | ecause the applicant failed to suggest a figure.  |   |
| be   | ecause this figure better characterizes the inver   | าชอก.   |

#### NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

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## INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international poulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 45.2).

Where a demand for international preliminary examination has been its filed, see below.

#### Haw?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

## NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
   \*Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
   daims 30, 33 and 35 unchanged; new claims 49 to 51 added.\*
- [Where originally there were 15 claims and after amendment of all claims there are 11]: \*Claims 1 to 15 replaced by amended claims 1 to 11.\*
- 3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
  "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
  "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

#### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

## Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

# Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide

## INTERNATIONAL SEARCH REPORT

Int conal application No.

PCT/US 98/08838

# Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: 1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claim(s) 1-4,7-10,12 partially and 5,6,11,14-19 completely is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet) This International Searching Authority found multiple inventions in this international application, as follows: As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which lees were paid, specifically claims Nos.: No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: The additional search fees were accompanied by the applicant's protest. Remark on Protest No protest accompanied the payment of additional search fees.

## TER HONAL SEARCH REPORT

ntern 1 Application No PCT/US 98/08838

| A. CLASSIF    | FICATION OF SUBJECT MATTER A61K38/55 G01N33/50   |  |                         |
|---------------|--|--|-------------------------|
|               |  | ~ <i>\$</i> .  | . '                     |
| According to  | International Patent Classification (IPC) or to both national classification               | on and IPC   |                         |
| B. FIELDS     |  |  |                         |
| Minimum do    | cumentation searched (classification system followed by classification $A61K$              | symbols)   |                         |
|               |  |  |                         |
| Documentati   | ion searched other than minimumdocumentation to the extent that suc                        | h documents are included in the fields sea   | rched                   |
|               |  |  |                         |
| Electronic da | ata base consulted during the international search (name of data base                      | and, where practical, search terms used)   |                         |
|               | •  |  |                         |
|               |  |  |                         |
|               |  |  |                         |
|               | ENTS CONSIDERED TO BE RELEVANT   |  | Relevant to claim No.   |
| Category *    | Citation of document, with Indication, where appropriate, of the relev                     | ant passages   | Tresevant to Claim 110. |
| Α.            | WO 94 03055 A (US HEALTH ;UNIV TUI   | FTS (US))  | 1-19                    |
|               | see page 4, line 9 - page 6, line  | 27   |                         |
|               | see page 8 - page 9; example 4   |  | ,                       |
| A             | พูก 91 17767 A (NEW ENGLAND MEDICA   | L CENTER   | 1-19                    |
| ^`            | INC :UNIV TUFTS (US)) 28 November  | 1991   |                         |
|               | see page 1, line 16 - page 3, line   | e 11   |                         |
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| X Furt        | ther documents are listed in the continuation of box C.                                    | X Patent family members are listed   | in annex.               |
| • Special ca  | ategories of cited documents :   | T" later document published after the Inte   | rnational filing date   |
| "A" docum     | ent defining the general state of the art which is not                                     | or priority date and not in conflict with<br>cited to understand the principle or th                                     | eory underlying the     |
| "E" earlier   |  | invention "X" document of particular relevance; the cannot be considered novel or canno                                  | claimed invention       |
| filing filing | ent which may throw doubts on priority claim(s) or   | involve an inventive step when the do  | cument is taken alone   |
| citatio       | on or other special reason (as specified)  | "Y" document of particular relevance; the<br>cannot be considered to involve an ir<br>document is combined with one or m | ore other such docu-    |
|               | nent referring to an oral disclosure, use, exhibition or means                             | ments, such combination being obvious in the art.  | ous to a person skilled |
|               | ent published prior to the international filing date but<br>than the priority date claimed | *&" document member of the same patent   |                         |
| Date of the   | actual completion of the international search  | Date of mailing of the international se-   | arch report             |
|               | 5 August 1998  | 13/08/1998   |                         |
| Name and      | mailing address of the ISA   | Authorized officer   |                         |
|               | European Patent Office, P.B. 5818 Patentiaan 2<br>NL - 2280 HV Rijswijk                    |  |                         |
|               | Tel. (-31-70) 340-2040, Tx. 31 651 epo nl.<br>Fax: (+31-70) 340-3016                       | Sitch, W   |                         |

## TER TIONAL SEARCH REPORT

PCT/uS 98/08838

| Category * Ci | AMINO<br>DIPEP<br>EXAMI<br>FUNCT<br>PROCE<br>SCIEN                           | KE E<br>PEPT<br>TIDE<br>NE T<br>ION"<br>EDIN<br>CES,<br>88,<br>5780<br>age | T AL:<br>IDASE<br>S AND<br>HE RO<br>USA<br>1991<br>25<br>1556 | : "'E IV<br>D US<br>OLE (<br>F TH | INHI<br>(DP<br>E OF<br>OF D | BITIO<br>-IV)<br>THES<br>P-IV<br>TIONA<br>1556- | ON OF<br>BY X<br>SE IN<br>IN T | DIP<br>(AA-B<br>HIBI<br>-CEL | PEPTID<br>BOROPR<br>TORS<br>L | YL<br>O<br>TO |    |   |   | 1-19 |    |  |
|---------------|--|--|---|-----------------------------------|-----------------------------|---|--------------------------------|------------------------------|-------------------------------|---------------|----|---|---|------|----|--|
| A -           | AMINO<br>DIPEP<br>EXAMI<br>FUNCT<br>PROCE<br>SCIEN<br>VOl.<br>XPOOD<br>see p | PEPT<br>TIDE<br>NE T<br>ION"<br>EDIN<br>CES,<br>88,<br>5780<br>age         | IDASE<br>S AND<br>HE RO<br>GS OF<br>USA<br>1991<br>25<br>1556 | E IV<br>D US<br>OLE (<br>F TH     | (DP<br>E OF<br>OF D<br>E NA | THES  | BY X<br>SE IN<br>IN T          | AA-B<br>HIBI<br>-CEL<br>ADEM | OROPR<br>TORS<br>L            | 0<br>TO       |    |   |   | 1-19 |    |  |
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ITE. TIONAL SEARCH REPORT

Information on patent family members

Interi al Application No PCT/US 98/08838

| Patent document cited in search report |   | Publication date |      | atent family<br>member(s) | Publication date |
|--|---|------------------|------|---------------------------|------------------|
| WO 9403055                             | Α | 17-02-1994       | AU   | 4794393 A                 | 03-03-1994       |
| WO 9117767                             | Α | 28-11-1991       | NONE |                           |                  |

## PAIENT COOPERATION TREATY



From the INTERNATIONAL SEARCHING AUTHORITY

To:

# **PCT**

| WOLF, GREENFIELD & SACKS, P.C. Attn. PLUMER, E. 600 Atlantic Avenue Boston, Massachusetts 02210 UNITED STATES OF AMERICA   | NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION  (PCT Rule 44.1)                 |  |  |  |
|--|--|--|--|--|
|  | Date of mailing (day/month/year) 01/09/1998  |  |  |  |
| Applicant's or agent's file reference  |  |  |  |  |
| IO254/7006WO   | FOR FURTHER ACTION See paragraphs 1 and 4 below  |  |  |  |
| International application No.  | International filing date  |  |  |  |
| PCT/US 98/08723  | (day/month/year) 30/04/1998  |  |  |  |
| Applicant  |  |  |  |  |
| TRUSTÉES OF TUFTS COLLEGE  |  |  |  |  |
| The applicant is hereby notified that the International Search   | Report has been established and is transmitted herewith.   |  |  |  |
| Filling of amendments and statement under Article 19 The applicant is entitled, if he so wishes, to amend the claims   | s of the International Application (see Rule 46):  |  |  |  |
| When? The time limit for filing such amendments is normal  |  |  |  |  |
| Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.35  | File Folder 10 01/98 DE MITE  Electronic Codo Book D  Docket Entry 10/148 D  |  |  |  |
| For more detailed instructions, see the notes on the accord  | npanying sheet. Docket Cross Off Order Copies  |  |  |  |
| 2. The applicant is hereby notified that no International Search Article 17(2)(a) to that effect is transmitted herewith.  |  |  |  |  |
| 3. With regard to the protest against payment of (an) addition   | al fee(s) under Rule 40.2, the applicant is notified that:   |  |  |  |
| the protest together with the decision thereon has been applicants's request to forward the texts of both the pro  | transmitted to the International Bureau together with the test and the decision thereon to the designated Offices. |  |  |  |
| no decision has been made yet on the protest; the appl   | icant will be notified as soon as a decision is made.  |  |  |  |
| 4. Further action(s): The applicant is reminded of the following:  |  |  |  |  |
| Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postponepublication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.— |  |  |  |  |
| Within 19 months from the priority date, a demand for international wishes to postpone the entry into the national phase until 30 months.  |  |  |  |  |
| Within 20 months from the priority date, the applicant must perfor<br>before all designated Offices which have not been elected in the<br>priority date or could not be elected because they are not bound   | e demand or in a later election within 19 months from the  |  |  |  |
| Name and mailing address of the International Searching Authority  | Authorized officer   |  |  |  |
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  | Véronique Baillou  |  |  |  |

| Name and mailing address of the International Searching Authority   | Authorized officer |
|---|--------------------|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Véronique Baillou  |

#### NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the International preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

#### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 45.2).

Where a demand for international preliminary examination has been its filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

#### NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended, it must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled:
- (iii) the claim is new;
- (N) the claim replaces one or more claims as filed:
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
   "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
   "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: \*Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added.\*

#### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preterably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

#### Consequence if a demand for international proliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

## PATENT COOPERATION TREAT 1

# PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference I0254/7006W0                                     | FOR FURTHER see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.   |   |  |
|--|---|---|--|
| International application No.  | International filing date (day/month/year)  | (Earliest) Priority Date (day/month/year)                   |  |
| DCT/US 00/00722  |   |   |  |
| PCT/US 98/08723 Applicant  | 30/04/1998  | 07/05/1997  |  |
| TRUSTEES OF TUFTS COLLEGE  |   |   |  |
| This International Search Report has been according to Article 18. A copy is being tra | n prepared by this International Searching Au<br>unsmitted to the International Bureau.   | uthority and is transmitted to the applicant                |  |
| This International Search Report consists  [X]. It is also accompanied by a copy       | y of each priorart document cited in this repo  | ort.  |  |
| Certain claims were found uns  | searchable(see Box I).  | •   |  |
| 2. Unity of invention is lacking (s  | ee Box II).   |   |  |
| international search was carried   | ntains disclosure of a nucleotide and/or ami<br>out on the basis of the sequence listing<br>with the international application.<br>ished by the applicant separately from the int<br>but not accompanied by a statement to<br>matter going beyond the disclosure in the | ternational application, the effect that it did not include |  |
| Tran   | nscribed by this Authority  |   |  |
|  | text is approved as submitted by the applicantext has been established by this Authority to   |   |  |
| USE OF CD26 INHIBITOR HIV  | FOR THE MANUFACTURE OF A  | MEDICAMENT FOR THE TREATMENT OF                             |  |
| 5. With regard to the abstract,  | · · · · · · · · · · · · · · · · · · ·   |   |  |
|  | text is approved as submitted by the applicar   | nt  |  |
| Box  | text has been established, according to Rule<br>III. The applicant may, within one month froi<br>rch Report, submit comments to this Authori  | mthe date of mailing of this International                  |  |
| 6. The figure of the drawings to be publi  | ished with the abstract is:   | <u>_</u> .  |  |
|  | suggested by the applicant.   | X None of the figures.                                      |  |
| · <b>=</b>   | ause the applicant failed to suggest a figure.  |   |  |
| beca   | ause this figure better characterizes the inver   | ntion.  |  |

INTERNATIONAL SEARCH REPORT

Intem. .al application No.

PCT/US 98/08723

Box III TEXT OF THE ABSTRACT (Continuation of Item 5 of the first sheet)

The use of a molecule that inhibits CD26 for the preparation of a medicament for increasing the immune response of a human patient infected with HIV, by contacting the T-cells, in vitro or in vivo, with the said molecule at a concentration effective to cause T-cell proliferation, but below an amount that causes detectable cytotoxicity.

| A. CLASSI   | FICATION OF SUSJECT MATTER   |   |                       |  |  |
|---|--|---|-----------------------|--|--|
| ÎPC 6   | FICATION OF SUBJECT MATTER A61K31/69 A61K38/55   |   |                       |  |  |
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| According to  | John Stand Court Claud Court and the North Standard Court Standard | · · · · ·   |                       |  |  |
|   | International Fatent Classification (IPC) or to both national classifica<br>SEARCHED   | tion and IPC  |                       |  |  |
| <del></del>   | cumentation searched (classification system followed by classification   | n symbols)  |                       |  |  |
| IPC 6   | A61K   |   |                       |  |  |
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| Documentat  | ion searched other than minimum documentation to the extent that su  | ich documents are included in the fields sean   | ched                  |  |  |
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| Electronic d  | ata base consulted during the international search (name of data bas   | se and, where practical, search terms used)   |                       |  |  |
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| C. DOCUM  | ENTS CONSIDERED TO BE RELEVANT   |   |                       |  |  |
| Category •  | Citation of decument, with indication, where appropriate, of the refe  | vant passages   | Relevant to claim No. |  |  |
|   |  |   |                       |  |  |
| x   | WO 94 03055 A (THE GOVERNMENT OF   | THE   | 1-13                  |  |  |
| •   | UNITED STATES OF AMERICA)) 17 Feb  |   | • • •                 |  |  |
|   | 1994   |   |                       |  |  |
|   | cited in the application   | ·   |                       |  |  |
|   | see page 1-12  |   |                       |  |  |
|   | see claims 1-26  | •   | :                     |  |  |
| X   | WO 95 29691 A (GEORGIA TECH RESEA  | RCH CO.)  | 1-13                  |  |  |
|   | 9 November 1995  |   | - 10                  |  |  |
| ]   | cited in the application   |   |                       |  |  |
|   | see the whole document   |   |                       |  |  |
| l <sub>x</sub>  | NO 80 03333 & (BACHOVCHIN N. N. N. S   | O Annil   | 1-13                  |  |  |
| ^   | WO 89 03223 A (BACHOVCHIN W.W.) 2<br>1989  | O April   | 1-12                  |  |  |
|   | cited in the application   |   |                       |  |  |
|   | see the whole document   |   |                       |  |  |
|   |  | ,   |                       |  |  |
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| X Funi  | ner documents are listed in the continuation of box C.   | X Patent family members are listed in   | annex.                |  |  |
| * Special ca  | tegories of cited documents:   | "T" later document published after the intern   | ational filing date   |  |  |
|   | ent defining the general state of the art which is not   | or priority date and not in conflict with the cited to understand the principle or theo |                       |  |  |
| considered to be of paracular relevance invention   |  |   |                       |  |  |
| filing date cannot be considered novel or cannot be considered to   |  |   |                       |  |  |
| which is cited to establish the publication date of another  "Y" document of particular relevance; the claimed invention  |  |   |                       |  |  |
| citation or other special reason (as specified)  Cannot be considered to involve an inventive step when the document referring to an oral disclosure, use, exhibition or document is combined with one or more other such document. |  |   |                       |  |  |
| other means ments, such combination being obvious to a person skilled in the art.  *P* document published prior to the international filing date but  |  |   |                       |  |  |
| later than the priority date daimed "&" document member of the same patent family   |  |   |                       |  |  |
| Date of the actual completion of the international search  Date of mailing of the international search report   |  |   |                       |  |  |
| 1   | 10 August 1998 01/09/1998  |   |                       |  |  |
| Name and r  | Name and mailing address of the ISA Authorized officer   |   |                       |  |  |
|   | European Patent Office, P.B. 5818 Patentlaan 2<br>NL • 2280 HV Rijswijk  |   |                       |  |  |
|   | Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,   | Economou, D   |                       |  |  |

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### INTERN ONAL SEARCH REPORT

erna' Application No PCT/US 98/08723

|            | ·   | PC1/US 98 | / 08/23               |
|------------|---|-----------|-----------------------|
| •          | ation) DOCUMENTS CONSIDERED TO BE RELEVANT  |           |                       |
| Category * | Citation of document, with indication, where appropriate, of the relevant passages  |           | Relevant to claim No. |
| X          | WO 93 08259 A (NEW ENGLAND MEDICAL CENTER HOSPITALS INC.) 29 April 1993 cited in the application see the whole document   |           | 1-13                  |
| X          | US 5 296 604 A (MILES INC.) 22 March 1994 cited in the application see the whole document   |           | 1–13                  |
| X          | WO 92 12140 A (GEORGIA TECH RESEARCH CO.) 23 July 1992 cited in the application see the whole document  |           | 1-13                  |
| <b>X</b>   | COUTTS S.J. ET AL.: "Structure-Activity Relationships of Boronic Acid Inhibitors of Dipeptidyl Peptidase IV.1. Variation of the P2 Position of Xaa-boroPro Dipeptides" J.MED.CHEM., vol. 39, no. 10, 10 May 1996, USA, pages 2087-2094, XP002074031 see page 2087, left-hand column, line 1 - page 2087, right-hand column, paragraph 2 see abstract  |           | 1-13                  |
| P,X        | JIANG J.D. ET AL.: "Inhibition of uman immunodeficiency virus type 1 infection in a T-cell line (CEM) by new dipeptidyl-peptidase IV (CD26) inhibitors" RES.VIROL, vol. 148, no. 4, July 1997 - August 1997, FRANCE, pages 255-266, XP002074032 see page 258, left-hand column, paragraph 5 - page 264, left-hand column, line 41 see figure 1 see page 255; left-hand column, line 1 - page 256, right-hand column, line 20 see abstract |           | 1-13                  |
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SEARCH REPORT

Information on patent family members

rnati pplication No PCT/US 98/08723

| Patent document cited in search repo | rt  | Publication date |                                  | atent family<br>nember(s)   | Publication date   |
|--------------------------------------|-----|------------------|----------------------------------|---|--|
| WO 9403055                           | Α   | 17-02-1994       | AU                               | 4794393 A   | 03-03-1994   |
| WO 9529691                           | . A | 09-11-1995       | US                               | 5543396 A   | 06-08-1996   |
| WO 8903223                           | Α   | 20-04-1989       | US<br>AU<br>DK<br>FI             | 4935493 A<br>2801289 A<br>658489 A<br>900101 A                            | 19-06-1990<br>02-05-1989<br>22-12-1989<br>09-01-1990                             |
| WO 9308259                           | Α   | 29-04-1993       | CA<br>EP<br>JP<br>US             | 2121369 A<br>0610317 A<br>7504158 T<br>5462928 A                          | 29-04-1993<br>17-08-1994<br>11-05-1995<br>31-10-1995                             |
| US 5296604                           | Α   | 22-03-1994       | NONE                             |   |  |
| WO 9212140                           | A   | 23-07-1992       | AU<br>AU<br>CA<br>EP<br>JP<br>US | 654834 B<br>9155391 A<br>2098702 A<br>0564561 A<br>6504547 T<br>5257901 A | 24-11-1994<br>17-08-1992<br>29-06-1992<br>13-10-1993<br>26-05-1994<br>02-11-1993 |

# PATENT COOPERATION . REATY

From the INTERNATIONAL SEARCHING AUTHORITY PCT To: PAUL T. CLARK FISH & RICHARDSON 225 FRANKLIN STREET NOTIFICATION OF TRANSMITTAL OF BOSTON, MASSACHUSETTS 02110-280-THE INTERNATIONAL SEARCH REPORT 00.398 OR THE DECLARATION (PCT Rule 44.1) Date of Mailing Date of Mailing (day/month/year) 03 FEB 1993 Applicant's or agent's file reference See paragraphs 1 and 4 below FOR FURTHER ACTION International application No. International filing date (day/month/year) 21 OCTOBER 1992 PCT/US92/09206 Applicant NEW ENGLAND MEDICAL CENTER HOSPITALS, INC. The applicant is hereby notified that the international search report has been established and is transmitted herewith. 1. X Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46): The time limit for filing such amendments is normally 2 months from the date of transmittal or the international search report; however, for more details, see the notes on the accompanying sheet Where? To the International Bureau of WIPO 34, chemin des Colombettes PCTSH .... 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the accompanying sheet. The applicant is hereby notified that no international search report will be established and that the declara-Article 17(2)(a) to that effect is transmitted herewith. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that the protest together with the decision thereon has been transmitted to the International Bureau together with a applicant's request to forward the texts of both the protest and the decision thereon to the designated O::... no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made The applicant is reminded of the following: 4. Further action(s): Shortly after 18 months from the priority date, the international application will be published by the International linear. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, he: completion of the technical preparations for international publication. Within 19 months from the priority date, a demand for international preliminary examination must be filed if the 4;, . . . : wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even. . . Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national. before all designated Offices which have not been elected within 19 months from the priority date or could not I. . because they are not bound by Chapter II. Authorized officer Name and mailing address of the ISA/ VSH LESTER L. LEE Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Telephone No. (703) 308-0196

Form PCT/ISA/220 (July 1992)\*

Facsimile No. NOT APPLICABLE

(See notes on accom? .

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PATENT COOPERATION ...EATY

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# INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference                         | FOR FURTHER ACTION                                      | see Notification of (Form PCT/ISA/220 below. | Transmittal of International Search Report  1) as well as, where applicable, item 5          |
|---|---|--|--|
| 00398/037WO2<br>International application No.                 | International filing dat                                |  | (Earliest) Priority Date   |
| PCT/US92/09206  | 21 OCTOBER 1992   |  | 22 OCTOBER 1991  |
| FC110372107200  |   |  |  |
| Applicant NEW ENGLAND MEDICAL CENTE                           | R HOSPITALS, INC.                                       |  |  |
| This international search report consist                      | ts of a total of sheet                                  | ts.  | thority and is transmitted to the applicant  . report.                                       |
| X It is also accompanied by a                                 | copy of each prior art do                               |  |  |
| 1. Certain claims were found                                  | •   | 1).  |  |
| 2. Unity of invention is lacking                              | ng (See Box II).  |  |  |
| 3. The international application international search was car | on contains disclosure of<br>ried out on the basis of t | f a nucleotide and/o<br>he sequence listing  | or amino acid sequence listing and the   |
|   | filed with the internation                              | nal application.                             |  |
|   | 6 -ished by the applica                                 | ant senerately from th                       | e international application,   |
|   |   | t. d but a clater                            | nent to the effect that it did not include matter<br>the international application as filed. |
|   | transcribed by this Auth                                | hority.                                      |  |
| 4. With regard to the title, X                                | the text is approved as                                 | submitted by the app                         | licant.  |
|   | the text has been establ                                | lished by this Authori                       | ity to read as follows:  |
|   |   |  |  |
|   |   |  |  |
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|   |   |  | •  |
| 5. With regard to the abstract,                               | the text is approved as                                 | submitted by the app                         | olicant.   |
|   |   |  | - · an art his bis bis as single as a discussion   |
| . <u>x</u>  | in Box III. The appli<br>international search re        | icant may, within on<br>port, submit commen  | the month from the date of mailing of this to this Authority.                                |
| 6. The figure of the drawings to be                           | e published with the abst                               | ract is:                                     |  |
| 6. The figure of the drawings to be Figure No                 | as suggested by the a                                   | splicant.                                    | X None of the figures  |
| ,,  | because the applicant                                   |  |  |
| 片   | because this figure he                                  | tter characterizes the                       | invention.   |
|   | occause mis rigure no                                   |  |  |

# IN. ANATIONAL SEARCH REPORT

International application No. PCT/US92/09206

| A. CLASSIFICATION OF SUBJECT MATTER  IPC(5) :A61K 37/02; C07K 5/06, 5/08, 5/10  US CL :514/18, 19; 530/330, 331  US CL :514/18, 19; 530/330, 331 |   |            |  |                                    |
|--|---|------------|--|------------------------------------|
|  | According to International Patent Classification (IPC) or to both national classification and IPC  B. FIELDS SEARCHED                 |            |  |                                    |
|  | ocumentation searched (classification system followed   | by classi  | ication symbols)   |                                    |
|  | 514/18, 19; 530/330, 331  | •          |  |                                    |
| Documentat   | ion searched other than minimum documentation to the  | extent tha | t such documents are included  | in the fields searched             |
|  |   |            |  |                                    |
| Electronic d   | ata base consulted during the international search (nar   | ne of data | base and, where practicable  | , search terms used)               |
| C. DOC   | UMENTS CONSIDERED TO BE RELEVANT  |            |  |                                    |
| Category*  | Citation of document, with indication, where app  | propriate, | of the relevant passages   | Relevant to claim No.              |
| Y  | US, A, 4,935,493 (BACHOVCHIN) 19 June 1990,   | see the e  | ntire document.  | 1-6                                |
| A  | US, A, 4,318,904 (SHAW ET AL.) 09 March 1983  | e, see abs | tract.   | 1-6                                |
| A  | US, A, 4,999,082 (SHENVI ET AL.) 12 February 1985, see Abstract. 1-6  |            |  |                                    |
| Α .  | US. A, 4,582,821 (KETTNER ET AL.) 15 April 1986, see Abstract.  |            |  | 1-6                                |
| A  | US. A. 4,636,492 (KETTNER ET AL.) 13 January 1987, see Abstract.  |            | 1-6  |                                    |
| Α  | US, A, 4,652,552 (KETTNER ET AL.) 24 March  | 1987, sec  | Abstract.  | 1-6                                |
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| Furt   | I her documents are listed in the continuation of Box C   |            | See patent family annex.   |                                    |
| • s <sub>s</sub>   | pecial categories of cited documents:   | •т•        | later document published after the is  | ication but cited to understand an |
| .V. q  | comment defining the general state of the art which is not considered<br>be part of particular relevance                              | -x-        | principle or theory underlying the i   | the elaimed invention cannot be    |
|  | rlier document published on or after the international filing date<br>ocument which may throw doubts on priority claim(s) or which is | ^          | when the document is taken alone   | dered to involve an invenior sup   |
| ci<br>Bp   | ted to establish the publication date of another citation or other electial reason (as specified)                                     | •ч•        | document of particular relevance;<br>considered to involve an inventi<br>combined with one or more other a | uch documents, such combination    |
| • • • • • • • • • • • • • • • • • • •  | ocument referring to an oral disclosure, use, exhibition or other cans  |            | being obvious to a person skilled in<br>document member of the same pate                                   | the art                            |
| Ů.   | ocument published prior to the international filing date but later than<br>the priority date claimed                                  | ٠«.        | mailing of the international s   |                                    |
| Date of the  | actual completion of the international search   | Date of    |  |                                    |
| 04 JANU  | JARY 1993   |            | 03FEB 1993   |                                    |
| Commissi   | mailing address of the ISA/<br>oner of Patents and Trademarks   |            | zed officer<br>STER L. LEE VSI   |                                    |
| Box PCT<br>Washingto   | on, D.C. 20231  |            |  |                                    |
|  | No. NOT APPLICABLE  | Telepho    | one No. (703) 308-0196   |                                    |
| Form PCT/  | ISA/210 (second sheet)(July 1992)*  |            |  |                                    |

International application No. PCT/US92/09206

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The abstract is too long, PCT Rule 4.3.

ABSTRACT OF THE DISCLOSURE

The invention is drawn to potent inhibitors of the enzymatic activity of DP-IV wherein the inhibitors are -amino boronic acid analogs of protein.

## IN ATIC AL SEARCH REPORT

International application No. PCT/US92/09206

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The abstract is too long, PCT Rule 4.3.

ABSTRACT OF THE DISCLOSURE

The invention is drawn to potent inhibitors of the enzymatic activity of DP-IV wherein the inhibitors are -amino boronic acid analogs of protein.

Form PCT/ISA/210 (continuation of first sheet(2))(July 1992) •

# IN. ANATIONAL SEARCH REPORT

International application No.
PCT/US92/09206

|               |  |            |   | 1   |
|---------------|--|------------|---|---|
| A. CLASS      | SIFICATION OF SUBJECT MATTER   |            |   |   |
| IPC(5) :A     | 61K 37/02; C07K 5/06, 5/08, 5/10   | al alassi  | fication and IPC  |   |
| According to  | 14/18, 19; 530/330, 331 International Patent Classification (IPC) or to both nation  | 41 Class.  |   |   |
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| Minimum doc   | OS SEARCHED cumentation system followed by commentation searched (classification system followed by commentation system system followed by commentation system  |            |   |   |
|               | 40 520/220 221   |            |   | in the fields searched  |
|               | on searched other than minimum documentation to the exter  | nt that si | ich documents are included  | El tile tieles secreties  |
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|               | ata base consulted during the international search (name o   | f data b   | ase and, where practicable,   | search terms used)  |
| Electronic da | ata base consulted during the international search (name o   |            |   |   |
|               |  |            |   |   |
|               |  |            |   |   |
| C. DOC        | UMENTS CONSIDERED TO BE RELEVANT .   |            |   | Relevant to claim No.   |
|               | Citation of document, with indication, where appropriate the control of the contr | oriate, o  | f the relevant passages   |   |
| Category*     | Change 1990 see  | the ent    | ire document.   | 1-6   |
| Y             | US, A, 4,935,493 (BACHOVCHIN) 19 June 1990, sec  |            |   | 1-6   |
| A             | US, A, 4,318,904 (SHAW ET AL.) 09 March 1982, s  | ee absti   | act.  |   |
|               | ·  |            |   | 1-6   |
| A             | US, A, 4,999,082 (SHENVI ET AL.) 12 February 19  | 85, 500    | Work and a second | 1-6   |
|               | US. A, 4,582,821 (KETTNER ET AL.) 15 April 198   | 6, sec A   | bstract.  |   |
| ^             | US. A. 4,636,492 (KETTNER ET AL.) 13 January 1   | 987, sc    | e Abstract.   | 1-6   |
| A             | US, A, 4,636,492 (KETTNER ET AC.)  | .07        | Abstract  | 1-6   |
| A             | US, A, 4,652,552 (KETTNER ET AL.) 24 March 19  | 187, 500   | Austra  |   |
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| -             | urther documents are listed in the continuation of Box C.  |            | See patent family anne  | a serious data are priority   |
| <u> </u>      | Special categories of cited documents:   | ·T·        | later document published after to<br>date and not in conflict with the  | he international filing date or priority application but eited to understand the he invention |
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| .F.           |  | ٠٠.        | e - miculae releva  | nce; the claimed invention cannot to  |
| '             | cited to establish the publication   | -1         | COUNCELED AN TITLE  | her such documents. Such com  |
| .0.           | document referring to an oral disclosure, use, exhibition or outer   |            | combined with one or more of<br>being obvious to a person skill<br>document member of the same  |   |
| P.            | means document published prior to the international filing date but later than   | ٠۴.        | document member of the service  | nal search report   |
|               | the priority date claimed  f the actual completion of the international search   | Date       | of mailing of the internation   | )   |
| 1             |  |            | 03FEB 1993  | 3i  |
| 04 J          | ANUARY 1993  | 3.016      | orized officer  | /   |
| Name          | and mailing address of the ISA/  | 1          | ESTER L. LEE  | VSH J   |
| Com           | nmissioner of Fatelia and Town   | l l        | 000 010   | 96  |
| Was           | mile No. NOT APPLICABLE  | Tele       | phone No. (703) 308-019   |   |

# PATENT COOPERATION TREATY



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| Attn. PLUMER, E. File Folder   |  |  |  |  |
|  | (PCT Rule 44.1)  |  |  |  |
| UNITED STATES OF AMERICA Order Copies  | 2)   |  |  |  |
| - Annuilles<br>Confirmation  |  |  |  |  |
|  | Date of mailing (day/month/year) 23/02/1999  |  |  |  |
|  | (day/month/year) 23/02/1999  |  |  |  |
| Sio reference  | FOR FURTHER ACTION See paragraphs 1 and 4 below  |  |  |  |
| Applicant's or agent's file reference I0248/7005W0   |  |  |  |  |
| International application No.  | International filing date (day/month/year) 29/09/1998  |  |  |  |
| PCT/US 98/20343  |  |  |  |  |
| Applicant  |  |  |  |  |
| i  |  |  |  |  |
| POINT THERAPEUTICS, INC.   | this bod and is transmitted herewith.  |  |  |  |
| The service of the se | ch Report has been established and is transmitted herewith.  |  |  |  |
| and statement and statement and the claim  | ims of the international Paper   |  |  |  |
| The applicant is entitled, if he so wishes, toalliers and  | acity 2 months from the date of transmittal of the   |  |  |  |
| The applicant is entitled, if he so wishes, toanierid the distriction of the solution of the s | nally 2 months from the date of transmittal of steel details, see the notes on the accompanying sheet  |  |  |  |
| Annahoral Bureau of WIPO   |  |  |  |  |
| Where? Directly to the International Bureau of Will 34, chemin des Colombettes 1211 Geneva 20, Switzerland   |  |  |  |  |
| 5 accimule No : (41-22) /40 1-   |  |  |  |  |
| For more detailed instructions, see the notes on the av  | companying sneet.  |  |  |  |
| used that no International Sa  | arch Report will be established and that the declaration under   |  |  |  |
|  |  |  |  |  |
|  | dditional fee(s) under Rule 40.2, the applicant is notified that:  seen transmitted to the International Bureau together with the  |  |  |  |
| 3. With regard to the protest against payment of (an) as   | ignification is the international Bureau together with the   |  |  |  |
| the protest together with the decision thereon has   | been transmitted to the International Bureau together with the protest and the decision thereon to the designated Offices.   |  |  |  |
| applicants s request to to the second  | ut a colling as soon as a decision is made.  |  |  |  |
| no decision has been made yet on the protest; th   | e applicant will be notified as soon as a decision is made.  |  |  |  |
| · ·  |  |  |  |  |
| 4. Further action(s): The applicant is reminded of the follow  | onal application will be published by the International Bureau.  |  |  |  |
| 4. Further action(s): The applicant is reminded of the following:  Shortly after 18 months from the priority date, the international application will be published by the International Bureau.  Shortly after 18 months from the priority date, the international application will be published by the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the lift the applicant wishes to avoid or postpone publication, a provided in Rules 90bis.1 and 90bis.3, respectively, before the lift the applicant must reach the International Bureau as provided in Rules 90bis.1  |  |  |  |  |
| eriority claim, must reach the International Dublication.  |  |  |  |  |
| completion of the same a demand for inte   | rnational preliminary examination of the priority date (in some Offices even later).   |  |  |  |
| wishes to postpone the entry into the national phase until   | ernational preliminary examination must be filed if the applicant is 30 months from the priority date (in some Offices even later).  If you may be a compared to the present of the priority of the present of the prese |  |  |  |
| the provint date, the approver.  |  |  |  |  |
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| A the Japanational Searching Au  | thority Authorized officer   |  |  |  |
| Name and mailing address of the International Searching Au   | Barbara Klaver   |  |  |  |

Barbara Klaver

European Patent Office, P.B. 5818 Patentlaan 2

NL-2280 HV Rijswijk

Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.

Fax: (+31-70) 340-3016

#### NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

# INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international politication. Furthermore, it should be emphasized that provisional protection is available in some States only.

## What parts of the International application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

#### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

#### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2)

Where a demand for international preliminary examination has been/is filed, see below.

#### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

# NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in the letter must more are differences between the claims as filed and the claims as amended, it must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- the claim is unchanged;
- the claim is cancelled; (ii)
- the claim is new; (iii)
- the claim replaces one or more claims as filed; (iv)
- the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]: \*Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- [Where originally there were 15 claims and after amendment of all claims there are 11]: Claims 1 to 15 replaced by amended claims 1 to 11.
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding \*Claims 1 to 6 and 14 unchanged, claims 7 to 13 cancelled; new claims 15, 16 and 17 added.\* or \*Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged.
- Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended [Where various kinds of amendments are made]: claim 14; claim 17 subdivided into amended claims 15, 15 and 17; new claims 20 and 21 added.

The amendments may be accompanied by a statement explaining the amendments and indicating any impact "Statement under article 19(1)" (Rule 46.4) that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1))

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended it must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim

# Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination is, as the time of ming any amendments under which 15, a demand for meritanental premission of the amendments with the has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preiminary Examining Authority (see Rule 62.2(a), first sentence)

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the daims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PATENT COOPERATION 1 REATY

# PCT

# INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference I0248/7005W0                                   | FOR FURTHER see Notification of (Form PCT/ISA/2  | f Transmittal of International Search Report<br>(20) as well as, where applicable, item 5 below. |
|--|--|--|
| International application No.  | International filing date (day/month/year)   | (Earliest) Priority Date (day/month/year)  |
| PCT/US 98/20343  | · 29/09/1998   | 29/09/1997   |
| Applicant  |  |  |
| POINT THERAPEUTICS, INC.   |  |  |
| This International Search Report has bee according to Article 18. A copy is being tr | en prepared by this International Searching Aut<br>ansmitted to the International Bureau.  | hority and is transmitted to the applicant   |
| This International Search Report consist  It is also accompanied by a cop            | s of a total of <u>3</u> sheets.<br>by of each prior art document cited in this repor  | t.   |
| 1. Certain claims were found u   | nsearchable(see Box I).  |  |
| 2. Unity of invention is lacking   | (see Box II).  |  |
| 3. X The international application contempt international search was carried         | ontains disclosure of a nucleo tide and/or amiled out on the basis of the sequence listing   | no acid sequence listing and the   |
| X file   | ed with the international application.   |  |
| ful  | rnished by the applicant separately from the int   | ernational application.  |
|  | but not accompanied by a statement to matter going beyond the disclosure in the  | ne international application as filed.   |
| Tr   | anscribed by this Authority  |  |
| 4. With regard to the title, X th  | e text is approved as submitted by the applica   | nt .   |
| th   | e text has been established by this Authorityto  | read as follows:   |
|  |  |  |
| 5. With regard to the abstract,  |  |  |
|  | ne text is approved as submitted by the applica<br>ne text has been established, according to Rule   | 38 2/h) by this Authority as it appears in   |
|  | ne text has been established, according to his<br>lox, III. The applicant may, within one month for<br>learch Report, submit comments to this Author | All the date of thaming of the   |
| 6. The figure of the drawings to be p  | ublished with the abstract is:   |  |
| Figure No a  | s suggested by the applicant.  | None of the figures.   |
|  | ecause the applicant failed to suggest a figure  |  |
|  | pecause this figure better characterizes the invo  | enion.   |
|  |  | ·  |

Form PCT/ISA/210 (first sheet) (July 1992)

# INTERNATIONAL SEARCH REPO!

International Application No PCT/US 98/20343

| A. CLASSIF  | ICATION OF SUBJECT MATTER<br>C12N5/08  |   |                       |
|---|--|---|-----------------------|
| J   |  |   | ,                     |
| According to  | International Patent Classification (IPC) or to both national classificatio  | n and IPC   |                       |
| B. FIELDS   | SEARCHED   |   |                       |
| Minimum do  | cumentation searched (classification system followed by classification searched) ${\sf C12N}$  | symbols)  |                       |
|   | ion searched other than minimum documentation to the extent that such  |   |                       |
| Electronic d  | ata base consulted during the international search (name of data base  | and, where practical, search terms used)  |                       |
| C DOCUM   | ENTS CONSIDERED TO BE RELEVANT   |   |                       |
| Category '  | Creation of document, with indication, where appropriate, of the relev   | ant passages  | Relevant to claim No. |
| A   | WO 94 03055 A (THE GOVERNMENT OF T<br>UNITED STATES OF AMERICA) 17 Febru<br>cited in the application<br>see the whole document       | THE<br>Jary 1994  | 1-30                  |
| A   | BRISTOL L A ET AL: "Inhibition of enzyme activity with pro-boropro stimulates rat granulocyte/macroph colony formation and thymocyte |   | 1-30                  |
|   | proliferation in vitro." BLOOD, (1995 JUN 15) 85 (12) 3602- XP002092855 see the whole document                                       | -9,   |                       |
| X Fu  | ther documents are listed in the continuation of box C.  | X Patent family members are liste   | d in annex.           |
| 'Special categories of cited documents:  "A" document betining the general state of the land which is not considered to be of particular relevance. "E" earlier occument but published on or after the international filing date.  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified). "O" document referring to an oral disclosure, use, exhibition or other means. "P" document published prior to the international filing date but |  | <ul> <li>T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</li> <li>"X" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is taken alone</li> <li>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</li> </ul> |                       |
| late  | r than the priority date dialined  | "&" document member of the same pate:  Date of mailing of the international s   |                       |
| Date of th  | ne actual completion of the international search  10 February 1999   | 23/02/1999  |                       |
| Name ar   | ed making address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2   | Authorized officer  |                       |
|   | NL - 2280 HV Rijswijk<br>Tal (+31-70) 340-2040, Tx. 31 651 epo nl.<br>Fax (+31-70) 340-3016  | Moreau, J   |                       |

### INTERNATIONAL SEARCH REPO

International Application No
PCT/US 98/20343

| Category * | ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| A          | COUTTS S J ET AL: "Structure-activity relationships of boronic acid inhibitors of dipeptidyl peptidase IV. 1. Variation of the P2 position of Xaa-boroPro dipeptides."  JOURNAL OF MEDICINAL CHEMISTRY, (1996 MAY 10) 39 (10) 2087-94, XP002092856 see the whole document | 1-30                  |
| A          | ANSORGE S ET AL: "CD26 /dipeptidyl peptidase IV in lymphocyte growth regulation." ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1997) 421 127-40, XP002092857 see the whole document  | 1-30                  |
|            |   |                       |
|            | · .   |                       |
|            |   |                       |
|            |   |                       |

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### INTERNATIONAL SEARCH REPC

Information on patent family members

International Application No
PCT/US 98/20343

| Patent document cited in search report |   | Publication date |    | atent family<br>nember(s) | Publication<br>date |
|--|---|------------------|----|---------------------------|---------------------|
| WO 9403055                             | Α | 17-02-1994       | AU | 4794393 A                 | 03-03-1994          |
|  |   |                  |    |                           |                     |

### PATENT COOPERATION TREATY



# From the INTERNATIONAL SEARCHING AUTHORITY

# To:

WOLF GREENFIELD & SACKS, P.C.

NOTIFICATION OF TRANSMITTAL OF

| 600 Atlantic Avenue Federal Reserve Plaza Boston, Massachusetts 02210 UNITED STATES OF AMERICA  | THEIN   |                      | CLARATION le 44.1)         |  |
|---|---|----------------------|----------------------------|--|
|   | Date of mailing (day/month/year)                | 29/07/199            | 99                         |  |
| Applicant's or agent's file reference   | FOR FURTHER A                                   | ACTION See           | e paragraphs 1 and 4 below |  |
| I0248/7007W0  |   |                      | s paragraphs i and i belen |  |
| International application No. PCT/US 99/ 10777  | International filing day/month/year)            | ate<br>14/05/199     | 99                         |  |
|   | <u> </u>  |                      | DOCKETED                   |  |
| POINT THERAPEUTICS, INC.  |   |                      | AUG 0 5 1999               |  |
| The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.  Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):  When? The time limit for filing such amendments is normally 2 months from the date of transmitted of the International Search Report; however, for more details, see the notes on the accompanying sheet.  Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.35  For more detailed instructions, see the notes on the accompanying sheet.  The applicant is hereby notified that no International Search Report will be established after Copies And 17(2)(a) to that effect is transmitted herewith.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:  the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  In odecision has been made yet on the protest; the applicant will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90 <i>bis</i> .1 and 90 <i>bis</i> .3, respectively, before the completion of the technical preparations for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later). |   |                      |                            |  |
| Within 20 months from the priority date, the applicant must perform before all designated Offices which have not been elected in the priority date or could not be elected because they are not bound   | rm the prescribed act<br>le demand or in a late | s for entry into the | national phase             |  |
|   |   |                      |                            |  |

Name and mailing address of the International Searching Authority

European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Authorized officer

Maurizio Amodeo

1 . .

### NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been is filed, see below.

### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

### NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled:
- (iii) the claim is new:
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

# The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
   \*Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added.\*
- [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
   "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
   "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### Consequence if a demand for international preliminary examination has already been filed.

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the international Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62:2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be turnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PATENT COOPERATION TREATY

# **PCT**

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference  | FOR FURTHER See Notificat (Form PCT/II)   | ion of Transmittal of International Search Report<br>SA/220) as well as, where applicable, item 5 below.   |  |  |
|--|---|--|--|--|
| International application No.  | International filing date (day/month/year   | (Earliest) Priority Date (day/month/year)  |  |  |
| PCT/US 99/10777  | 14/05/1999  | 05/06/1998   |  |  |
| POINT THERAPEUTICS, INC.   |   |  |  |  |
| This International Search Report consists  | nsmitted to the International Bureau.   | Authority and is transmitted to the applicant this report.   |  |  |
| Basis of the report  |   |  |  |  |
| a. With regard to the language, the i  | nternational search was carried out on the<br>ess otherwise indicated under this item.  | basis of the international application in the  |  |  |
| the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).                                  |   |  |  |  |
| was carried out on the basis of the  contained in the internation  filed together with the inter  furnished subsequently to  the statement that the subsinternational application as | sequence listing: nal application in written form. national application in computer readable this Authority in written form. this Authority in computer readble form. sequently furnished written sequence listin filed has been furnished. | to international application, the international search form.  In does not go beyond the disclosure in the rm is identical to the written sequence listing has been |  |  |
| Certain claims were foun     Unity of invention is lack  | d unsearchable (See Box I).<br>ing (see Box II).  |  |  |  |
| 4. With regard to the title,  X the text is approved as sub the text has been establish  | mitted by the applicant.<br>ed by this Authority to read as follows:  |  |  |  |
| 5. With regard to the abstract,  | •   |  |  |  |
| the text is approved as sub  | ed, according to Rule 38.2(b), by this Auth   | nonty as it appears in Box III. The applicant may, report, submit comments to this Authority.  |  |  |
| 6. The figure of the drawlngs to be publis  as suggested by the applicate because the applicant failed   | ent.  | None of the figures.   |  |  |
| because this figure better c   | haracterizes the invention.   | •  |  |  |

### INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/10777

| Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)   |
|---|
| This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:  |
| 1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claims 39-42, 44-50 are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the compound/composition. RULE 39.1(iv) PCT Method of treatment of the human/animal body by therapy  2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).   |
| Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)   |
| This International Searching Authority found multiple inventions in this international application, as follows:   |
|   |
| As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  |
| 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.   |
| 3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:   |
| 4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:   |
| Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.   |

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 39-42,44-50 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Claims Nos.: 39-42,44-50

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

### INTERN. IONAL SEARCH REPORT

Information on patent family members

intern. ,al Application No PCT/US 99/10777

| Patent document cited in search report  US 4935493 A 19-06-1990 AU 2801289 A 02-05-1989 DK 658489 A 22-12-1989 FI 900101 A 09-01-1990 W0 8903223 A 20-04-1989  WO 9310127 A 27-05-1993 AU 661362 B 20-07-1995 AU 3136893 A 15-06-1993 CA 2123128 A 27-05-1993 CN 1073946 A 07-07-1995 EP 0641347 A 08-03-1995 FI 942345 A 20-05-1994 HU 67937 A 29-05-1995 JP 7501078 T 02-02-1995 MX 9206628 A 01-05-1993 |           |              |           |     |           |            |
|--|-----------|--------------|-----------|-----|-----------|------------|
| DK 658489 A 22-12-1989 FI 900101 A 09-01-1990 W0 8903223 A 20-04-1989  W0 9310127 A 27-05-1993 AU 661362 B 20-07-1995 AU 3136893 A 15-06-1993 CA 2123128 A 27-05-1993 CN 1073946 A 07-07-1993 CZ 9401244 A 12-07-1995 EP 0641347 A 08-03-1995 FI 942345 A 20-05-1994 HU 67937 A 29-05-1995 JP 7501078 T 02-02-1995   |           |              |           |     |           |            |
| FI 900101 A 09-01-1990 W0 8903223 A 20-04-1989  W0 9310127 A 27-05-1993 AU 661362 B 20-07-1995 AU 3136893 A 15-06-1993 CA 2123128 A 27-05-1993 CN 1073946 A 07-07-1993 CZ 9401244 A 12-07-1995 EP 0641347 A 08-03-1995 FI 942345 A 20-05-1994 HU 67937 A 29-05-1995 JP 7501078 T 02-02-1995  | US 493549 | A 19-06-1990 | 1935493 A |     | 2801289 A | 02-05-1989 |
| WO 8903223 A 20-04-1989  WO 9310127 A 27-05-1993 AU 661362 B 20-07-1995  |           |              |           | DK  | 658489 A  | 22-12-1989 |
| WO 9310127 A 27-05-1993 AU 661362 B 20-07-1995 AU 3136893 A 15-06-1993 CA 2123128 A 27-05-1993 CN 1073946 A 07-07-1995 CZ 9401244 A 12-07-1995 EP 0641347 A 08-03-1995 FI 942345 A 20-05-1994 HU 67937 A 29-05-1995 JP 7501078 T 02-02-1995  |           |              |           | FI  | 900101 A  | 09-01-1990 |
| AU 3136893 A 15-06-1993 CA 2123128 A 27-05-1993 CN 1073946 A 07-07-1993 CZ 9401244 A 12-07-1995 EP 0641347 A 08-03-1995 FI 942345 A 20-05-1994 HU 67937 A 29-05-1995 JP 7501078 T 02-02-1995   |           |              |           | WO  | 8903223 A | 20-04-1989 |
| AU 3136893 A 15-06-1993 CA 2123128 A 27-05-1993 CN 1073946 A 07-07-1993 CZ 9401244 A 12-07-1995 EP 0641347 A 08-03-1995 FI 942345 A 20-05-1994 HU 67937 A 29-05-1995 JP 7501078 T 02-02-1995   | WO 931012 | A 27-05-1993 | 9310127 A | LIA | 661362 B  | 20-07-1995 |
| CA 2123128 A 27-05-1993 CN 1073946 A 07-07-1993 CZ 9401244 A 12-07-1995 EP 0641347 A 08-03-1995 FI 942345 A 20-05-1994 HU 67937 A 29-05-1995 JP 7501078 T 02-02-1995   |           |              |           |     |           |            |
| CN 1073946 A 07-07-1993<br>CZ 9401244 A 12-07-1995<br>EP 0641347 A 08-03-1995<br>FI 942345 A 20-05-1994<br>HU 67937 A 29-05-1995<br>JP 7501078 T 02-02-1995  |           |              | _         |     |           |            |
| CZ 9401244 A 12-07-1995<br>EP 0641347 A 08-03-1995<br>FI 942345 A 20-05-1994<br>HU 67937 A 29-05-1995<br>JP 7501078 T 02-02-1995   |           | •            | ŕ         |     |           |            |
| EP 0641347 A 08-03-1995<br>FI 942345 A 20-05-1994<br>HU 67937 A 29-05-1995<br>JP 7501078 T 02-02-1995  |           |              |           |     |           |            |
| FI 942345 A 20-05-1994<br>HU 67937 A 29-05-1995<br>JP 7501078 T 02-02-1995   |           |              |           |     |           |            |
| HU 67937 A 29-05-1995<br>JP 7501078 T 02-02-1995   |           |              |           |     |           |            |
| JP 7501078 T 02-02-1995  |           |              |           |     |           |            |
|  |           |              |           |     |           |            |
| 11V 3500050 W 01-03-1333   |           |              |           |     |           |            |
| NO 941905 A 14-07-1994   |           |              |           |     |           |            |
|  |           |              |           |     |           |            |
| NZ 245207 A 26-07-1994   |           |              |           |     |           |            |
| PT 101079 A 28-02-1994   | •         |              |           |     |           |            |
| SK 59294 A 08-02-1995  |           |              |           |     |           |            |
| ZA 9208978 A 24-05-1993  |           |              |           | ZA  | 92089/8 A | 24-05-1993 |

# INTERNATIONAL SEARCH REPORT

International Application No PCT/US 99/10777

|   | .· ·· ·· ·· · · · · · · · · · · · · · ·  | - <u></u>  |                         |  |
|---|--|--|-------------------------|--|
| A. CLASS  | FICATION OF SUBJECT MATTER C07F5/02 A61K31/69  |  |                         |  |
| According to  | o International Patent Classification (IPC) or to both national classific  | cation and IPC   |                         |  |
|   | SEARCHED   | <u> </u>   |                         |  |
| Minimum de  | ocumentation searched (classification system followed by classificat   | ion symbols)   |                         |  |
| IPC 6   | CO7F A61K  |  |                         |  |
| Documenta   | tion searched other than minimum documentation to the extent that  | such documents are included in the fields se   | earched                 |  |
|   |  |  |                         |  |
| Electronic d  | ata base consulted during the international search (name of data ba  | ase and, where practical, search terms used  | )                       |  |
|   |  |  |                         |  |
| С РОСИМ   | ENTS CONSIDERED TO BE RELEVANT   | ·  |                         |  |
| Category *  | Citation of document, with Indication, where appropriate, of the re  | levani nassaces  | Relevant to claim No.   |  |
| Calegory  | oranon oraconners, war indication, where appropriate, or the re-   | ievan k passages   | TIGIGVAIN TO CIAMIT TO. |  |
| А   | US 4 935 493 A (BACHOVCHIN, W.W.<br>19 June 1990 (1990-06-19)<br>cited in the application<br>the whole document              | ET AL.)  | 1                       |  |
|   |  |  |                         |  |
| Α   | COUTTS, SIMON J. ET AL:  |  | 1                       |  |
|   | "Structure-Activity Relationships  |  |                         |  |
|   | Boronic Acid Inhibitors of Dipep<br>Peptidase IV. 1. Variation of the  |  |                         |  |
|   | Position of Xaa-boroPro Dipeptide  |  |                         |  |
|   | J. MED. CHEM. (1996), 39(10), 208<br>1996, XP002109442   |  |                         |  |
|   | 1990, XI 002109442   |  |                         |  |
|   | -  | -/   |                         |  |
|   |  |  |                         |  |
|   |  |  |                         |  |
|   |  |  |                         |  |
|   |  |  |                         |  |
|   |  |  |                         |  |
| X Furth   | ner documents are listed in the continuation of box C.   | X Patent family members are listed   | In annex.               |  |
| * Special cal   | tegories of cited documents:   | "T" later document published after the inte  |                         |  |
|   | ont defining the general state of the art which is not ered to be of particular relevance                                    | or priority date and not in conflict with cited to understand the principle or the invention |                         |  |
| "E" earlier d   | "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention |  |                         |  |
| "L" document which may throw doubts on priority claim(s) or involve an inventive step when the document is taken alone which is cited to establish the publication date of another  |  |  | cument is taken alone   |  |
| citation or other special reason (as specified)  Cannot be considered to involve an inventive step when the document referring to an oral disclosure, use, exhibition or document is combined with one or more other such docu-         |  |  |                         |  |
| other means ments, such combination being obvious to a person skilled in the art.  "P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family |  |  |                         |  |
|   | actual completion of the international search  | Date of mailing of the international sea   |                         |  |
| 16  | 5 July 1999  | 29/07/1999   |                         |  |
| Name and m  | nailing address, of the ISA  | Authorized officer   |                         |  |
|   | European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo ni,        | Pinkol   |                         |  |
|   | Fnx: (+31-70) 340-3016   | Rinkel, L  |                         |  |

# INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/10777

| CICarrie                  | NIAN) DOCUMENTS CONCINCIONA  | PCT/US 9 | 9/10///               |
|---------------------------|--|----------|-----------------------|
| C.(Continua<br>Category * | ation) DOCUMENTS CONSIDERED TO BE RELEVANT   |          |                       |
| Caregory                  | Citation of document, with indication, where appropriate, of the relevant passages   |          | Relevant to claim No. |
| A                         | SNOW, ROGER J. ET AL: "Studies on Proline Boronic Acid Dipeptide Inhibitors of Dipeptidyl Peptidase IV: Identification of a Cyclic Species Containing a B-N Bond" J. AM. CHEM. SOC. (1994), 116(24), 10860-9, 1994, XP002109443 cited in the application |          |                       |
| A                         | KELLY, TERENCE A. ET AL: "Immunosuppresive boronic acid dipeptides: correlation between conformatio and activity" J. AM. CHEM. SOC. (1993), 115(26), 12637-8 ,1993, XP002109444  |          | 1                     |
|                           | WO 93 10127 A (BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.) 27 May 1993 (1993-05-27) the whole document   |          | 1                     |
|                           | ·  |          |                       |
|                           |  |          |                       |
|                           |  |          |                       |
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|                           |  | ,        |                       |
|                           |  |          |                       |
|                           |  |          |                       |

### PATENT COOPERATION TREATY



From the INTERNATIONAL SEARCHING AUTHORITY

WOLF, GREENFIELD & SACKS, P.C.

NOTIFICATION OF TRANSMITTAL OF

| Attn. Plumer, Elizabeth Ř. 600 Atlantic Avenue Boston, Massachusetts 02210 UNITED STATES OF AMERICA  |  | OR THE DEC   |   |  |  |
|--|--|--|---|--|--|
|  | Date of mailing (day/month/year)   | 21/10/199  | 9   |  |  |
| Applicant's or agent's file reference I0248/7006W0   | FOR FURTHER ACTION   | ON See   | paragraphs 1 and 4 below  |  |  |
| International application No. PCT/US 99/09652  | International filing date (day/month/year)   | 3/05/199   | 9   |  |  |
| Applicant  |  |  | DOCKETED  |  |  |
| POINT THERAPEUTICS, INC.   |  |  | NOV 0 2 1999  |  |  |
| The applicant is entitled, if he so wishes, to amend the claim  When? The time limit for filling such amendments is normal International Search Report; however, for more det  Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41–22) 740.14.35  For more detailed Instructions, see the notes on the accordance of the Article 17(2)(a) to that effect is transmitted herewith.  | lly 2 months from the date alis, see the notes on the alis, see the notes on the alignment of the notes on the alignment of the notes o | of transmittal of accompanying  File Folder ECS ! Docket Entry Docket Cross of Order Copies Annuities Confirmation | of the sheet.   |  |  |
| With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:  the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.  no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.   |  |  |   |  |  |
| 4. Further action(s): The applicant is reminded of the following:  Shortly after 18 months from the priority date, the international applif the applicant wishes to avoid or postpone publication, a notice priority claim, must reach the International Bureau as provided in completion of the technical preparations for international publicat.  Within 19 months from the priority date, a demand for international wishes to postpone the entry into the national phase until 30 more.  Within 20 months from the priority date, the applicant must perform before all designated Offices which have not been elected in the | of withdrawal of the internal Rules 90bis. 1 and 90bis. 3 ion.  I preliminary examination naths from the priority date (ion) the prescribed acts for endemand or in a later election.  | ational applical 3, respectively  nust be filed if in some Office  ntry into the na                                | tion, or of the<br>, before the<br>the applicant<br>is even later). |  |  |
| priority date or could not be elected because they are not bound   | by Chapter II.   |  |   |  |  |

Name and mailing address of the International Searching Authority

European Patent Office, P.B. 5818 Patentiaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016

Claudia Aragone

### NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

### INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

### What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

### When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Bule 46.1).

### Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been is filed, see below.

### How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

### What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

### NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
   "Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
   claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
- [Where originally there were 15 claims and after amendment of all claims there are 11]:
   \*Claims 1 to 15 replaced by amended claims 1 to 11.\*
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims): "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- [Where various kinds of amendments are made]:
   Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

# Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

# Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be turnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

# PATENT COOPERATION TREATY

# PCT

# INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference  | (Form PCT/ISA/2  | of Transmittal of International Search Report<br>(20) as well as, where applicable, item 5 below. |  |  |  |  |
|--|--|---|--|--|--|--|
| I0248/7006WO   | ACTION   |   |  |  |  |  |
| International application No.  | International filing date (day/month/year)   | (Earliest) Priority Date (day/month/year)   |  |  |  |  |
| PCT/US 99/ 09652 03/05/1999 04/05/1998   |  |   |  |  |  |  |
| Applicant  |  |   |  |  |  |  |
|  |  |   |  |  |  |  |
| POINT THERAPEUTICS, INC.   |  |   |  |  |  |  |
| according to Article 18. A copy is being tra   |  | hority and is transmitted to the applicant  |  |  |  |  |
| This International Search Report consists  It is also accompanied by   | of a total of3 sheets. a copy of each prior art document cited in this                               | s report.   |  |  |  |  |
| Basis of the report  |  |   |  |  |  |  |
| a. With regard to the language, the  | international search was carried out on the baless otherwise indicated under this item.              | isis of the international application in the  |  |  |  |  |
| the international search w Authority (Rule 23.1(b)).   | ras carried out on the basis of a translation of t   |   |  |  |  |  |
|  | d/or amino acid sequence disclosed in the in sequence listing:                                       | nternational application, the international search  |  |  |  |  |
|  | onal application in written form.  |   |  |  |  |  |
|  | rnational application in computer readable for   | m.  |  |  |  |  |
| furnished subsequently to this Authority in written form.  |  |   |  |  |  |  |
| furnished subsequently to  | furnished subsequently to this Authority in computer readble form.                                   |   |  |  |  |  |
| the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished. |  |   |  |  |  |  |
| the statement that the info<br>furnished   | ormation recorded in computer readable form  | is identical to the written sequence listing has been   |  |  |  |  |
| 2. Certain claims were fou   | nd unsearchable (See Box I).   |   |  |  |  |  |
| 3. Unity of invention is lac   |  | ,   |  |  |  |  |
|  |  |   |  |  |  |  |
| 4. With regard to the title,   |  |   |  |  |  |  |
| the text is approved as su   |  |   |  |  |  |  |
| the text has been establis   | hed by this Authority to read as follows:  |   |  |  |  |  |
|  |  |   |  |  |  |  |
| _  |  |   |  |  |  |  |
| 5. With regard to the abstract,  |  |   |  |  |  |  |
| the text is approved as su   | bmitted by the applicant.  | •   |  |  |  |  |
| Aha taut has been establis   | thed, according to Rule 38.2(b), by this Author<br>a date of mailing of this international search re | rity as it appears in Box III. The applicant may, sport, submit comments to this Authority.       |  |  |  |  |
| 6. The figure of the drawings to be public   | lished with the abstract is Figure No.   |   |  |  |  |  |
| as suggested by the appli  |  | None of the figures.  |  |  |  |  |
| because the applicant fail   |  |   |  |  |  |  |
| because this figure better   | characterizes the invention.   |   |  |  |  |  |

### INTERNA? IAL SEARCH REPORT

Internation. pplication No PCT/US 99/09652

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 A61K31/69 A61K A61K38/55 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61K IPC 6 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category \* 1-4,7,WO 98 50046 A (TUFTS COLLEGE) P,X 22-29, 12 November 1998 (1998-11-12) 34,36, 38,39, 42-63 the whole document 22-27. WO 98 50066 A (TUFTS COLLEGE) P,X 29,34, 12 November 1998 (1998-11-12) 36,39, 42-63 the whole document Patent family members are listed in annex. Further documents are listed in the continuation of box C. "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the Special categories of cited documents: "A" document delining the general state of the art which is not considered to be of particular relevance invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to \*E\* earlier document but published on or after the international filing date involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-particular and particular and particula "O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. \*&\* document member of the same patent family document published prior to the international filing date but later than the priority date claimed Date of mailing of the international search report Date of the actual completion of the international search 21/10/1999 15 October 1999 **Authorized officer** Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2

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NL – 2280 HV Rijswijk Tel. (+31-70) 340–2040, Tx. 31 651 epo nl, Fax: (+31-70) 340–3016

Hoff, P

# INTERNAT IAL SEARCH REPORT

PCT/US 99/09652

|           | ation) DOCUMENTS CONSIDERED TO BE RELEVANT  | Relevant to claim No.                           |
|-----------|---|---|
| ategory * | Citation of document, with indication, where appropriate, of the relevant passages  |   |
| (         | WO 94 03055 A (US HEALTH ;UNIV TUFTS (US)) 17 February 1994 (1994-02-17) cited in the application   | 8-13,15,<br>22-27,<br>29,34,<br>36,39,<br>42-63 |
|           | the whole document  |   |
| (         | WO 95 11689 A (TUFTS COLLEGE ;BACHOVCHIN<br>WILLIAM W (US)) 4 May 1995 (1995-05-04)   | 42-63   |
| 4         | the whole document  | 1-41  |
| X         | WO 93 08259 A (NEW ENGLAND MEDICAL CENTER<br>INC ;UNIV TUFTS (US))<br>29 April 1993 (1993-04-29)  | 42-63   |
| A         | the whole document  | 1-41  |
| <b>A</b>  | BRISTOL L A ET AL: "Inhibition of CD26 enzyme activity with pro-boropro stimulates rat granulocyte/macrophage colony formation and thymocyte proliferation in vitro" BLOOD, vol. 85, no. 12, 15 June 1995 (1995-06-15), pages 3602-3609, XP002092855 ISSN: 0006-4971 the whole document                             | 1-41  |
| A         | COUTTS S J ET AL: "Structure-activity relationships of boronic acid inhibitors of dipeptidyl peptidase IV. 1. Variation of the P2 position of Xaa -boroPro dipeptides"  JOURNAL OF MEDICINAL CHEMISTRY, vol. 39, no. 39, 10 May 1996 (1996-05-10), pages 2087-2094, XP002092856  ISSN: 0022-2623 the whole document | 1-41  |
| A         | WO 98 00439 A (TUFTS COLLEGE ;BACHOVCHIN WILLIAM W (US)) 8 January 1998 (1998-01-08) the whole document   | 1-63  |
| Ρ,Α       | WO 99 16864 A (POINT THERAPEUTICS INC) 8 April 1999 (1999-04-08) the whole document   | 1-63  |
|           | Tegas TA  |   |
|           |   |   |
|           |   |   |

1

### INTERNATIONAL SEARCH REPORT

Information. patent family members

Internation plication No PCT/US 99/09652

| Patent document cited in search report | Publication<br>date | Patent family membe <u>r(</u> s)                             | Publication<br>date                                  |
|--|---------------------|--|--|
| WO 9850046 A                           | 12-11-1998          | AU 7269198 A   | 27-11-1998   |
| WO 9850066 A                           | 12-11-1998          | AU 7274798 A   | 27-11-1998   |
| WO 9403055 A                           | 17-02-1994          | AU 4794393 A   | 03-03-1994   |
| WO 9511689 A                           | 04-05-1995          | NONE   |  |
| WO 9308259 A                           | 29-04-1993          | CA 2121369 A<br>EP 0610317 A<br>JP 7504158 T<br>US 5462928 A | 29-04-1993<br>17-08-1994<br>11-05-1995<br>31-10-1995 |
| WO 9800439 A                           | 08-01-1998          | AU 3792797 A<br>CA 2258038 A<br>EP 0938498 A                 | 21-01-1998<br>08-01-1998<br>01-09-1999               |
| WO 9916864 A                           | 08-04-1999          | AU 9588798 A   | 23-04-1999   |

# . ATENT COOPERATION TREAT

by fax and post From the: INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY To: PLUMER, Elizabeth R. WOLF, GREENFIELD & SACKS, P.C. WRITTEN OPINION 600 Atlantic Avenue Boston, Massachusetts 02210 (PCT Rule 66) ETATS-UNIS D'AMERIQUE 22 10,99 617 720 2441 Date of mailing (day/month/year) within 1 month(s) REPLY DUE from the above date of mailing Applicants or agent's file reference 10248/7005WO Priority date (day/month/year) International filing date (day/month/year) International application No. 29/09/1997 29/09/1998 PCT/US98/20343 International Patent Classification (IPC) or both national classification and IPC Applicant POINT THERAPEUTICS, INC. 1. This written opinion is the first drawn up by this International Preliminary Examining Authority. 2. This opinion contains indications relating to the following items: Basis of the opinion O Non-establishment of opinion with regard to novelty, inventive step and industrial applicability Priority н □ Lack of unity of invention Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, Inventive step or industrial applicability; 1V citations and explanations supporting such statement ☐ Certain document cited ☐ Centain defects in the international application VII Certain observations on the International application 3. The applicant is hereby invited to reply to this opinion. See the time limit indicated above. The applicant may, before the explication of that time limit, request this Authority to grant an extension, see Rule 68.2(d). When? By submitting a written repty, accompanied, where appropriate, by amendments, according to Rule 66.3.

For the form and the language of the amendments, see Rules 66.8 and 66.9. How?

For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or orguments, see Pule 66.4 bis.

For an informal communication with the examiner, see Rule 66.6.

It no reply is filled, the international preliminary examination report will be established on the basis of this opinion.

 The final data by which the international preliminary examination report must be established according to Rule 69.2 is: 29/01/2000.

Name and mailing address of the international preliminary examining authority:



Also:

#U. UNI. 1995 19.00

European Palent Office D-80298 Munich Tel. +49 89 2399 • O Tx: 523656 epmu d Fax: +49 89 2399 • 4465

Authorized officer / Examiner

Kalsner, I

Formalities officer (Incl. extension of time limits) Vullo, C

Telephone No. +49 89 2399 8061



Form PCTAPEA/403 (cover sheet) (January 1994)

# WRITTEN OPINION

I. Basis of the opinion

International application No. PCT/US98/20343

| ١. | Basis of the obturou  | turnished to the receiving Office   |  |  |
|----|---|---|--|--|
| 1. | Basis of the opinion.<br>This opinion has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office<br>in response to an invitation under Article 14 are referred to in this opinion as "originally filed".): |   |  |  |
|    | Doscription, pages:   |   |  |  |
|    | 1-43  | as originally filed   |  |  |
|    | Claims, No.:  |   |  |  |
|    | 1-30  | as originally filed   |  |  |
|    | Drawings, sheets:   |   |  |  |
|    | 1/5-5/5   | as originally filed   |  |  |
|    |   |   |  |  |
| 2  | . The amendments hav  | ve resulted in the cancellation of:   |  |  |
|    | ☐ the description,  | pages:  |  |  |
|    | the claims,   | Nos.:   |  |  |
|    | ☐ the drawings,   | sheets:   |  |  |
| ;  | 3. This opinion has bee considered to go bey  | n established as if (some of) the amendments had not been made, since they have been cond the disclosure as filed (Rule 70.2(c)): |  |  |
| •  | 4. Additional observation   | ns, if necessary:   |  |  |
|    |   |   |  |  |
|    |   | • 4   |  |  |

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

Form PCT/IPEA/408 (Boxes I-Vill, Sheet 1) (January 1994)

oxtimes paid additional fees under protest.

neither restricted nor paid additional fees.

IV. Lack of unity of invention

restricted the claims.

paid additional fees.

2. 

This Authority found that the requirement of unity of invention is not complied with for the following reasons

# WRITTEN OPINION

and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:

- 3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:
  - 🛛 all parts.
  - ☐ the parts relating to claims Nos. .
- V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- 1. Statement

Novelty (N)

10-12: no (1-9, 13-30: yes) Claims

Inventive step (IS)

13-17: no (1-9, 18-30: yes) Claims

Industrial applicability (IA)

Claims

- 2. Citations and explanations see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

soe separate sheet

# Ad Section V: Reasoned statement with regard to novelty, inventive step or industrial applicability

### 1) Documents

D1...WO-A-940305 D2...Bristol et al. (1995) Blood 85: 3602-3609

# INVENTION 1 (CLAIMS 1-17)

- 2) Novelty
- 2.1) Claims 10-12 do not meet the requirements of Art. 33(2) PCT.

Claim 10 is directed to an apparatus comprising a container and an inhibitor of dipeptidylpeptidase type IV (DPIV) contained therein or attached thereto.

Inhibitors of DPIV are known in the art. Hence, any container containing DPIV-inhibitors can be considered novelty destroying for claim 10.

Moreover, D1 discloses methods of culturing haematopoietic cells in the presence of DPIV inhibitor. Hence, claims 11 and 12 cannot be considered novel in view of D1, either.

- 2.2) Claims 1-9 relating to a method for stimulating haematopoietic cells in vitro, and claims 13-17 meet the requirements of Art. 33(2) PCT as the subject-matter of these claims is not disclosed as such in the available prior art.
- 3). Inventive step
- 3.1) Claim 13, which further defines the apparatus of claim 10, does not meet the requirements of Art. 33(3) PCT as it does not add any features which would render inventive the subject-matter of claim 10.
- 3.2) Claims 14 and 15 do not meet the requirements of Art. 33(3) PCT as a

composition of magnetic particles and DPIV inhibitor, both of which are known in the state of the art, are not considered to involve an inventive step.

- 3.3) Claims 16 and 17 relate to a kit for stimulating haematopoietic cells in vitro. Since it is known in the art that haematopoietic cells can be stimulated in the presence of DPIV inhibitors and corresponding experiments are disclosed, e.g. in D1, a kit comprising the means for stimulating haematopoietic cells cannot be considered to involve an inventive step in the sense of Art. 33(3) PCT.
- 3.4) Claims 1-9 are considered to meet the requirements of Art. 33(3) PCT.

Claim 1 is directed to a method for stimulating haematopoietic cells in vitro comprising culturing the haematopoietic cells in the presence of the inhibitor of DPIV and in the absence of exogenous cytokine.

Both D1 and D2 describe methods for stimulating haematopoietic cells using DPIV inhibitor. In both documents, however, media are disclosed which contain exogenous cytokines. The possibility of stimulating haematopoietic cells in the absence of cytokines is not disclosed or derivable in an obvious manner from these documents. Hence, claim 1 and the claims dependent thereon (claims 2-9) are considered to involve an inventive step in the sense of Art. 33(3) PCT.

INVENTION 2 (CLAIMS 18-30)

4) Novelty and inventive step

Claims 18-30 are considered to meet the requirements of Art. 33(2)(3) PCT as methods for expanding antigen-specific T cells *in vitro* comprising culturing early T lineage cells in the presence of a heteroconjugate containing an inhibitor of a DPIV inhibitor attached to an antigenic peptide are neither disclosed nor suggested in the prior art. (Note, however, the comments in Section VIIII)

Ad Section VIII: Certain observations on the international application

Claims 18-30 do not meet the requirements of Art. 5 and 6 PCT.



WRITTEN OPINION SEPARATE SHEET

> Claims 18-21 refer to a method for expanding antigen-specific T cells comprising culturing T-cells in the presence of a heteroconjugate containing an inhibitor of a DPIV inhibitor attached to an antigenic peptide.

> It is not clear, how an inhibitor of a DPIV inhibitor should contribute to the expanding of T-cells. As DPIV inhibitors are known to stimulate haematopoietic cells using an inhibitor of a DPIV inhibitor should rather prevent the stimulation of haematopoletic cells. As the same formulation is found in the specification (p. 36-38) and no specific examples are given which would show the actual effect of the claimed methods claims 18-21 and dependent claims 22-30 lack clarity and are not considered sufficiently supported by the description.